REGULATION OF CYCLOOXYGENASE IN MACRO- AND MICROVESSEL ENDOTHELIUM

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Addition of acidic fibroblast growth factor (FGF) to rabbit coronary microvessel endothelial (RCME) cells (as well as human lung microvessel endothelial cells) increases *de novo* synthesis of cyclooxygenase, the rat limiting enzyme in prostaglandin biosynthesis. In contrast, aFGF treatment of human umbilical vein endothelial (HUVE) cells does not increase cyclooxygenase synthesis: indeed prolonged treatment of HUVE with aFGF results in a decrease in cyclooxygenase activity. Recently a novel inducible cyclooxygenase (COX II) was cloned; therefore in the present study we evaluated the regulation of COX II in RCME and HUVE. aFGF induced COX II in RCME as demonstrated by Northern blotting and by immunoprecipitation. HUVE demonstrated a high basal expression of COX II and COX II was not induced further by aFGF. aFGF effects on COX II appear to be mediated by protein kinase C since (1) phorbol esters mimicked the effects of aFGF (2) aFGF induction of COX II mRNA was blocked by H-7, a specific protein kinase C inhibitor. A structurally related inactive analog, Ha-1004, did not reduce the effects of aFGF. These studies demonstrate functional heterogeneity in the regulation of cyclooxygenase by growth factors in endothelia derived from diverse sites.

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